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Overview of Biomedical Materials

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Biomedical materials are synthetic polymers, metals, ceramics, inorganics, and natural macromolecules (biopolymers), that are manufactured or processed to be suitable for use in or as medical devices or prostheses.[1] These materials typically come in contact with cells, proteins, tissues, organs, and organ systems. They can be implanted for long-term use, e.g., an artificial hip, or for temporary use, e.g., an intravenous catheter. Except in isolated cases when a material is used by itself, such as collagen injections for filling soft tissue defects, biomedical materials are used as a component in a medical device. The form of the material (perhaps a textile) how it interfaces (blood contacting, for instance), and its time of use will determine its required properties. A material's use needs to be viewed in the context of the total device and its interface with the body. One material property alone is unlikely to lead to a successful and durable device, but the failure to address a key property can lead to device failure. Until recently, medical-grade polymers, ceramics, inorganics, and metals were purified versions of commercial-grade materials. A variety of polymers, biopolymers, and inorganics is now being specifically developed for medical applications. Table I summarizes the types of biomedical materials.

Driving Forces for Development

Conflicting forces affect the biomedical materials industry: cost containment (for less expensive yet highly effective devices) vies with enhanced product design. This also involves ways to reduce the toxicity of certain polymers, particularly that due to plasticizers such as the phthalates found in polyvinyl chloride (PVC), and finding resins suitable for gamma irradiation. Gamma irradiation for sterilization is growing in popularity since it avoids the toxic residues that may occur with ethylene ox-

ide (EtO) sterilization. More generally, development is being driven by the need for new technologies that will allow a variety of devices to function more effectively.

Meeting Cost-Containment Demands

One of the easiest, most effective ways to reduce the cost of a medical device is to use less expensive resins and polymers. Lower cost resins could find applications in blood oxygenator housings, syringe components, intravenous sets, and hemodialyzers, among other devices. However, function and biocompatibility must not be compromised. Another approach is to add value to medical devices that reduce the cost of medical care by reduced complications and hospital stay. If the rate of infections is reduced, for example, then the length of hospitalization drops and the use of drugs to treat infections is obviated. Examples of value-added devices that will function by incorporating new biomedical materials include thromboresistant coatings for catheters, infection-resistant coatings for urinary catheters, and percutaneous connectors that form a tight seal with the skin and therefore reduce infection, e.g., peritoneal dialysis, indwelling catheters for cancer therapy, drivelines for the artificial heart, and vascular access for drug delivery or blood treatment, such as hemodialysis.

Enhancing Product Design

Some devices require new materials and technologies to function properly. For instance, new joint replacements with improved life spans are needed since current prostheses have a lifetime of only 10 to 15 years before failure. Improvements might include enhanced stress transfer to the bone, which can be achieved with designs that match each patient's bone shape, improved fixation to bone using bioactive

ceramic coatings, and the use of fiber composites which more closely match the mechanical properties of bone.

New types of sophisticated medical devices increasingly require interdisciplinary teams to address their many and varied design requirements. Many devices demand a systems approach, calling on the talents of biologists, materials scientists, mechanical engineers, chemists, and biomedical engineers. The design of a new small-diameter vascular graft for coronary artery applications demonstrates the diversity of requirements (Figure 1). Many design questions must be addressed, including graft compliance, dilation, degradation, thromboresistance, infection resistance, calcification, biocompatibility, cytotoxicity, and leachability. Testing must also address other questions: What is the long-term chronic response? Will it cause tissues to thicken and eventually occlude the device? How will the patient's health and the drugs he takes affect the graft's overall response? Human factors issues for the surgeon include suturability, conformability, and ease of handling in the operating room environment. All these issues must be considered in order to design a successful device.

Other research and development involves artificial muscles using polymeric gels contained within a sac for contraction; microsurgical devices for reconnecting arteries and nerves; tissue adhesives to replace sutures in microsurgical applications, such as limb reattachment; biomaterials that can be laser-welded to tissue; neural devices to enhance nerve regeneration; conductive polymers with improved properties over metallic electrodes; and a method of directly interfacing computer chips on electrodes to neural tissue.

Testing

There are a tremendous number of obstacles to successfully introducing a new biomedical material. Probably the most difficult to overcome are the regulatory requirements a company must satisfy before a device containing the new material can be sold. Assuming a company can make a device that works, it must be approved for commercial sale by the Food and Drug Administration (FDA). In the most basic sense, the materials composing the device, as fabricated and sterilized, must be nontoxic, noncarcinogenic, nonantigenic, and nonmutagenic—in other words, they must not hurt cells or have any side effects on the biologic system either locally or bodywide.

Implanted devices impose a new set of requirements biologically and from a ma-

terials view. The effect of a foreign body in the biologic system is essentially that of wound healing in the presence of a sterile foreign material. The outcome of this healing process can have profound implications on the success of a device and can depend on material properties such as texture, crystallinity, wettability, surface charge and chemistry, and cytotoxic leachables and degradation products. For example, percutaneous devices (devices that pass through the skin such as a central venous catheter) that do not form a permanent tissue seal will become infected due to the lack of an effective bacterial barrier.[2] In general, percutaneous devices do not form a permanent seal, or the seal breaks down over time due to tissue contraction, a long-term consequence of wound healing, or high shear stresses at the interface.

Some of the basic testing is described by a guideline for toxicity testing, *Tripartite Biocompatibility Guidance for Medical Devices*, which includes suggested tests (sensitization, hemocompatibility, and mutagenicity by device application). The guideline was prepared to be applicable in Canada, the United Kingdom, and the United States. The process of demonstrating that a device is safe and that it functions as intended may also include accelerated fatigue testing as well as animal testing. Long-term durability of a device is a function of the biostability of its components. Recent concern over the long-term stability of polyurethanes has resulted in new processes and materials that produce a more biostable substrate.[3] The device must be capable of sterilization without losing its properties, and it must be stable on the shelf for at least two years. Safety is also evaluated by determining the lack of side effects; for instance, excessive wear products leading to excessive inflammation. A device classified as potentially life threatening may require extensive animal testing to demonstrate that it is effective and functions in its intended fashion, e.g., an artificial joint provides the needed range of motion and is durable. After preclinical data is compiled, a controlled human-clinical study may be required to demonstrate safety and efficacy in humans prior to commercial release. The testing program can take anywhere from two to ten years and require a large investment of time and capital.

Design Requirements

The success of many medical devices relies heavily on the further development of materials that meet the physical and biological design requirements of the device. The required properties, a function of the

particular device, include bioactivity, biodegradability, infection resistance, and thromboresistance. Increasingly, modification of wound healing and biologic pathways to improve function will be performed by systemic or controlled drug delivery. This is already done for devices such as mechanical heart valves and the artificial heart by chronic anticoagulation (the use of blood thinners). Growth factors and modifiers of wound healing will be used to improve function by tissue incorporation

and adhesion.[4] Table II shows some current products and efforts using controlled drug delivery to improve device function.

Bioactivity

Bioactive materials actively participate in the biologic response. The desired response may be a surface free of thrombus or may be controlled fibrous tissue formation. For example, compliant and textured or porous noncytotoxic materials show minimal fibrous tissue formation.[5] Some

Material	Application
Nondegradable Synthetics— Commodity Polymers	
Polyamides	Sutures
Polycarbonates	Housing materials
Polyesters	Vascular grafts
Polyformaldehyde	Heart valve stents
Polyolefins	Sutures, mesh for hernia repair
Polyvinyl chloride	Tubing, blood bags
Nondegradable Synthetics— Value-Added Polymers	
Fluorocarbons	Vascular grafts
Hydrogels	Contact lenses, catheter coatings
Polyolefin elastomers	Tubing, artificial heart bladder
Polyurethanes	Catheters, artificial heart bladders
Silicones	Soft tissue reconstruction, tubing
Ultrahigh molecular weight polyethylene	Acetabular cup
Biodegradables	
Albumin, cross-linked	Vascular graft coatings, cell encapsulation
Collagen/gelatin, cross-linked	Soft tissue reconstruction, vascular graft coatings
Polyamino acids	Controlled release, cell adhesion peptides
Polyanhydrides	Controlled release
Polycaprolactones	Controlled release, bone plates
Polylactic/glycolic acid copolymers	Sutures, bone plates
Polyhydroxybutyrates	Controlled release, bone plates
Polyorthoesters	Controlled release, bone plates
Biologically Derived Materials	
Bovine carotid artery	Vascular grafts
Bovine ligaments	Ligaments
Bovine pericardium	Pericardial substitute, heart valves
Human umbilical vein	Vascular grafts
Porcine heart valve	Heart valves
Bioderived Macromolecules	
Chitosans	Experimental, wound dressing, controlled release
Collagen	Soft tissue injectables, coatings, wound dressing
Elastin	Experimental, coatings
Gelatin, cross-linked	Artificial heart bladder coating
Hyaluronic acid	Coatings, wound dressing, surgical non-adhesion

Table I: Biomedical Materials and Applications

(continued)

Table I Continued

Tissue Adhesives	
Cyanoacrylates	Wound closure, microsurgery
Fibrin glue	Vascular graft coating
Molluscan glue	Enhancement of cell adhesion
Metal and Metallic Alloys	
	Orthopedic and dental implants, vascular stents
Cobalt chrome molybdenum alloys	Heart valve stents
Nitinol alloys (shape memory alloys)	Orthopedic wire
Stainless steels	Orthopedic wire
Titanium and titanium alloys	Artificial heart housing, heart valve stents
Ceramics, Inorganics, and Glasses	
Aluminum, calcium, and phosphorous oxides	Degradable bone filler, enhanced bone growth
Bioglass®	Bioactive phosphorous calcium glass, orthopedic coating
Glass ceramics	Encapsulation of implantable medical electronics
High density alumina	Acetabular cup, ball of hip prosthesis
Hydroxyapatites	Bioactive ceramic, orthopedic coating, bone fillers
Carbons	
Glassy carbons	Fibers for orthopedic composites
Pyrolytic (low temperature isotropic) carbon	Heart valves, dental implants
Ultralow temperature isotropic carbon	Coatings on heat sensitive polymers
Passive Coatings	
Albumin	Thromboresistance
Alkyl chains	Adsorbs albumin for thromboresistance
Fluorocarbons	Reduced drag for catheters, thromboresistance
Hydrogels	Reduced drag for catheters, thromboresistance
Silica-free silicones	Thromboresistance, improved wound healing for soft tissue reconstruction
Bioactive Coatings	
Anticoagulants, e.g., heparin and hirudin	Thromboresistance
Antimicrobials	Infection resistance
Bioactive ceramics and glasses	Bone adhesion and formation; soft tissue adhesion
Cell adhesion peptides	Enhanced cell adhesion, epithelium, endothelium
Cell adhesion proteins	Enhanced cell adhesion, epithelium, endothelium
Negative Surface Charge	Thromboresistance
Thrombolytics	Thromboresistance

materials appear to have some inherent activity, e.g., some negatively charged surfaces containing ionic species such as carboxyls appear to actively participate in the degradation of complement components (an inflammatory pathway) resulting in improved compatibility of hemodialysis membranes.[6] Recent efforts have involved incorporating cell attachment sequences in biomaterials; for example, elastin-like sequences with peptide cell attachment sites have been synthetically produced.[7] Many of these cell attachment peptide sequences are based on arginine-glycine-aspartic acid.[8] Other developments include the immobilization of bioactive molecules to a surface, e.g., heparin.[9]

Bioactive ceramics and glasses form an intimate bond with surrounding tissue and, in the presence of calcified bony tissue, can enhance bone formation.[10] The nature of the oxide layer of these materials allows glycosaminoglycans to adsorb and provide the proper matrix for bone formation. In soft tissue, collagen appears to form directly in this matrix material and provide tight tissue seals. Bioactive ceramics are polycrystalline, covalently bonded, hard, opaque, and usually based on calcium phosphates, particularly hydroxyapatite. Titanium oxide also has a bioactive surface. Bioactive glasses are amorphous, transparent, and based on calcium phosphates, silicates, and sodium oxides. Some polyester elastomers show a similar ability to enhance bone formation,[11] though the mechanism has not been identified. Polyester elastomers have also shown enhanced adhesion of endothelial cells without pretreatment with adhesion proteins.[12]

Controlled delivery devices incorporating immobilized enzymes are under investigation in order to modify release rates.[13] The approach is to create a change in local pH when the enyzme reacts with the target molecule. For example, glucose oxidase results in a decreased pH by catalyzing the change of glucose to gluconic acid. The release rate of the drug can be modified either by a pH-related change in the polymer (like swelling) or a pH-dependent increase in the solubility of the drug, e.g., insulin.

Biodegradability

Materials that degrade slowly and predictably in the human body are useful in several medical applications, especially those serving a temporary function such as sutures, bone fixation devices related to reconstructive surgery, scaffolding for cells that recreate damaged or diseased organs, and controlled-release drug delivery devices.[14] Materials used in such applications include synthetic and natural polymers, ceramics, and ceramic-based composites.

In reconstructive surgery, biodegradable sutures hold a wound together until it is healed and are then resorbed by the body, reducing the risk of infection and eliminating the need to remove the sutures. The diverse mechanisms of biodegradation make biodegradable materials well suited for controlled-release drug delivery. Devices made of biodegradable materials can release drugs in predetermined, customized doses and can deliver certain classes of drugs (such as peptide- or protein-based drugs) that cannot be readily administered by other methods. In these devices, the biodegradable material is resorbed by the body as it releases the drug or after the drug has been released.

Biocompatibility
Leachables
Cytotoxicity
Hemolysis

Anastomosis
Suturability
Ease of handling
Size mismatch

Compliance Mismatch
Wave reflections
Shear stress
Stress concentrations
Turbulence

Secondary flows induced by curvature

Anastomosis
Stenosis due to
intimal hyperplasia

Patient Health
Anticoagulants
Drug regime

Material Properties
Surface chemistry
Texture and porosity
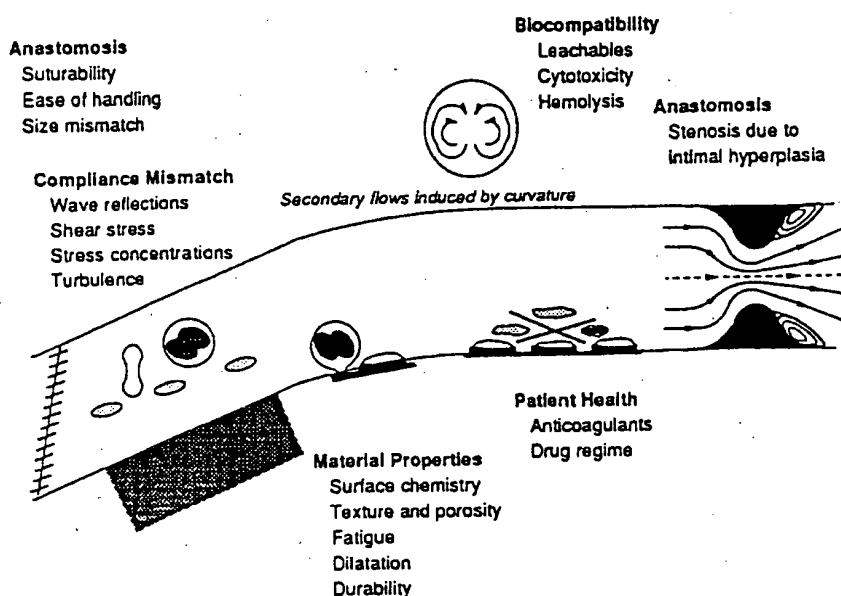Fatigue
Dilatation
Durability

Figure 1. Design considerations for a small diameter graft. Reprinted with permission, M.N. Helmus, Outlook for Biomedical Materials, DR Reports, Decision Resources, Inc., Dec. 1990.

Infection Resistance

The presence of a foreign body increases the risk of infection. Complications relating to infection include emboli, septicemia, coagulation of blood in the capillaries, the evolution of endotoxins from the walls of dead bacteria (which can lead to toxic shock), and enzymatic degradation of susceptible materials, particularly collagen-based prostheses.[15] The more virulent bacteria produce a slime or biofilm (consisting of proteins, polysaccharides, and glycoproteins) that interferes with the body's ability to fight infection. This film also makes the bacteria more resistant to antibiotic therapy, a particularly serious situation since many patients whose treatment requires medical devices are already immunocompromised.

With few exceptions, once a device-associated infection develops, the device must be removed. Infections related to the artificial heart limit the device to temporary use, usually by patients awaiting transplants. The artificial heart demonstrates infection-related complications resulting from the formation of septic emboli (blood clots containing bacteria that break off the surface of the device), infection along the skin-penetrating lines used to power the device, and blood damage caused by the mechanical and physiochemical mechanisms of the device that inhibit the body's ability to fight infection.

Approaches for reducing infection risks include the incorporation of antimicrobial agents (broad-spectrum chemicals and antibiotics) into the device; materials less prone to attachment of bacteria (some bacterial are less likely to adhere to wettable materials); materials that are not chronic activators of inflammation and complement (a complex series of enzymatic proteins that initiate an inflammatory process) since materials with high levels of activation do not fight infection as effectively; and devices that allow tissue incorporation by ingrowth into pores, which provides a bacterial barrier.

Thromboresistance

Thromboresistant materials are critical in the success or failure of devices that contact blood because the formation of blood clots on the surface of a device can block the patient's vascular system or clog the device itself. Also, materials that resist thrombus formation can make new procedures possible (such as temporary lung assists), and can reduce complications related to devices that remove blood from the body (such as blood oxygenators). Since the same thromboresistant material is not suitable for all medical applications, approaches to developing surfaces are based on whether the material will directly contact blood or damaged tissue. Research in this area is becoming more sophisticated

as better animal models and computer simulations become available, potentially shortening the timelines to commercialization for thromboresistant devices.

Polyester fabrics are an example of a material that works well for one application but not another. Polyester artificial arteries larger than 6 mm diameter function well since the larger volume of blood flowing in large arteries dilutes the thrombogenic factors released when the blood contacts the polyester artery.[1] But arteries smaller than 4 mm diameter have smaller volume flows and a larger relative surface area of implant exposed to the blood. The additional surface area in the smaller graft generates significantly more thrombogenic agents.

Designing materials for blood-contacting devices requires understanding the many competing reactions that occur when blood interacts with a foreign surface: protein adsorption, activation of blood enzymes, activation of the inflammatory pathways (particularly the complement pathway), adhesion and aggregation of blood platelets, fibrin formation, and attraction of white cells. Blood-contacting devices must function in conjunction with a complex feedback system in which enzymes in the blood can enhance or inhibit thrombosis formation, depending on which pathways predominate.[16]

Research has focused on surface properties and how they influence blood materials interactions. Surface properties under investigation include surface charge, surface energy (e.g., hydrophilic/hydrophobic character), mobile surfaces (molecules that have a high degree of surface mobility due to free segments, hydration, or lack of cohesion with the bulk), and domains/phase separation resulting in a repetitive surface heterogeneity on a molecular level.[17] Other efforts include incorporation of specific chemical entities, e.g., alkyl groups, or immobilization of bioactive agents.

Permeation and Diffusion

Permeation and diffusion are required in the design of membrane extracorporeal devices such as blood oxygenators and plasmapheresis devices, controlled drug delivery devices, and hybrid artificial organs. Transport of gases, nutrients, waste products, and bioactive molecules across the material/membrane is important in these applications.

Current extracorporeal devices are fabricated from hollow fibers. The use of small-diameter fibers (e.g., 0.2 mm diameter) increases surface area and reduces damage to blood in blood oxygenators by reducing exposure to air. An example of hollow fibers used in medical devices are

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the membranes in plasmapheresis devices, which are used to treat patients with autoimmune diseases. Blood from the patient passes through the first cartridge, and red blood cells are separated and returned to the patient. The remaining liquid plasma goes into a cooling unit, where the deviant immunoglobulins separate as cryoprecipitates. The plasma containing these cryoprecipitates then goes into the next cartridge, where the immunoglobulins causing the disease are removed, and the purified plasma is returned to the patient.[18]

Specialized applications for biomedical materials include hybrid artificial organs, membrane-encapsulated devices containing living cells that can be derived from an animal source and are designed to replace an organ function. An artificial pancreas, for example, would contain insulin-producing cells for treatment of diabetes. An artificial liver would contain hepatocytes to remove toxins from the blood in patients with acute liver failure. These devices would have very stringent design requirements: they must protect the cells from antibodies and white blood cells (the body's line of defense against foreign tissue), allow nutrients to permeate the cells, and remove waste byproducts while allowing enzymes produced by the cells and needed by the body to permeate. For example, insulin must be able to permeate out of the device in order to lower the high glucose levels of diabetics. In the artificial liver, high-molecular-weight enzymes cannot permeate through the membranes; if the molecular weight threshold of the membrane is raised, antibodies could attack the encapsulated cells. Also, special surface properties may be required of membranes to allow cells to adhere and function properly.[19]

Polymeric drug delivery systems are made by mixing or encapsulating the pharmaceutical with natural polymers, such as polysaccharides; or with synthetic polymers, such as silicone rubber and ethylene vinyl acetate copolymer; or with biodegradable ones, such as poly(lactide-co-glycolide). These devices—in the form of rods, cylinders, or flat slabs—can be placed under the skin, in the muscle, or in the abdominal cavity by a simple surgical procedure under local anesthesia. Matrix devices, formed by mixing the drug and polymer, are well suited for delivering drugs of low aqueous solubility, such as steroids, for periods of six months to two years. Reservoir devices, formed by encapsulating the drug within a polymeric controlled-release membrane, are well suited for delivering drugs of high aqueous solubility, such as luteinizing hormone-releasing hormone (LH-RH), over a shorter

term (less than six months). LH-RH is being used for cancer therapy.

Materials and Applications

Table I shows the wide variety of materials being used or considered for biomedical applications. Applications range from high-volume uses such as blood bags, wound dressings, and syringes to more invasive devices such as blood-contacting catheters and implantable devices (e.g., artificial hips and arteries), and to devices that replace organ function, such as the kidney and heart.[1] Commodity-oriented nondegradable synthetic polymers are used in such applications as tubing, hubs and connectors, heart valve stents, structural components of heart valves, housings for extracorporeal devices (e.g., blood oxygenators), and suture materials. PVC finds application as tubing and bags for storing blood and pharmaceuticals. The value of these materials is in their structural stability, relative biocompatibility, and low cost.

The value-added nondegradable synthetic materials provide enhanced properties such as drag reduction in cardiovascular catheters, which justifies using a more expensive polymer such as polytetrafluoroethylene or a hydrogel. Certain materials are available in specifically designated biomedical grades, which means that the company supplying them keeps a master file on their production and may certify basic biocompatability based on their being noncytotoxic. Polyether urea urethanes

are an example of a value-added polyurethane, which is used in the pumping bladder of the artificial heart. These materials have excellent fatigue properties and tear resistance, even though the same properties that give them such strength also dictate that they be solution cast rather than thermally formed.

Biodegradable biomedical materials are of high interest. Their ability to degrade gradually in the body makes them particularly appropriate for applications that do not require surgical removal. For biodegradable products to be useful, the breakdown products must be nontoxic; also, the body must have a mechanism for eliminating the byproducts.

Processed biologic tissue, animal or human tissue that has been treated to reduce antigenicity, typically includes arteries, veins, and ligaments. Initially, these materials tend to have excellent biocompatibility, but they degrade and calcify over five to ten years. Their durability has been improved by controlled chemical processing and cross-linking, particularly with gluteraldehyde, but lifetimes greater than 10 years still need to be demonstrated.

Purified biologic components are being developed for reproducibility and improved biocompatiblity with applications in reconstructive surgery and wound dressings. Recent efforts to produce genetically engineered proteins or polysaccharides from culture have two goals: improved mechanical properties and control of biologic interactions (e.g., to in-

Table I. Controlled Release to Improve Function of Medical Devices.

Medical Device	Controlled Release Method	Reason
Blood contacting catheters	Heparin release coating	Thrombosis
	Antibiotic/surfactant coating	Infection—blood and soft tissue
	Silver antimicrobial from cuff	Infection—soft tissue
Porcine heart valve	Anticalcifying drug from suture ring	Calcification of valve leaflets
Polyurethane wound dressing	Iodine or chlorhexidine antimicrobial	Infection of wound
Pacemaker electrode	Steroid from pacer tip	Excessive fibrous tissue around pacer tip
Urinary catheter	Silver antimicrobial in catheter wall	Infection
Bone cement	Antibiotics mixed into cement	Infection
Organoids formed in situ, e.g., liver	Growth factors	Induce new blood vessels and control of cell and tissue type

crease or decrease cellular interactions with the surface).

Tissue adhesives promise improved, rapid reattachment of blood vessels and nerves—particularly for microsurgical procedures such as limb reattachments.

Metals have found widespread application as biomedical materials for orthopedic and dental implants. Metals in use include austenitic stainless steels, cobalt chrome molybdenum alloys, titanium, and titanium alloys. Stainless steels are being replaced by the other alloys since the stainless alloys have limitations, including higher corrosion rates and release of nickel ions that can result in nickel hypersensitivity in many patients. Commercial state-of-the-art materials for orthopedic and dental implants are titanium and titanium alloys. They have excellent corrosion resistance and biocompatibility, and they are less stiff than stainless steel and cobalt chrome, which results in improved stress transfer to the bone. They also seem to be more biocompatible with bone. Titanium appears to bond directly to bone, and it has been suggested that the oxide layer on the surface of titanium is bioactive and induces new bone growth.

Ceramics, inorganics, and glasses have more limited but important applications as orthopedic and dental implants. High-density alumina is beginning to find use as the ball of the hip prosthesis. Bioactive ceramics and glasses—materials that can induce new bone growth and bond directly to bone—can be used to repair bone defects and to permanently attach a prosthesis to bone. Most bioactive ceramics and glasses are relatively brittle, and to be effective in high-stress applications they must be applied as a coating on high-strength materials such as titanium.

Carbons have been used in several biomedical applications because they are biocompatible, inert, and resist degradation. Pyrolytic carbons have been used in heart valves for their light weight, wear resistance, and relative thromboresistance.

Composite structures are used to develop devices with unique design requirements that can be met only by combining materials. Prostheses constructed of advanced composites have several advantages: (1) they can be made much lighter than metal implants, (2) their stiffness can be tailored to match the stiffness of the tissue, and (3) they can have biocompat-

ible surfaces on a substrate of desired mechanical properties.[20]

Biomedical coatings include such passive materials as silica-free silicones, hydrogels, and fluorocarbons. Glow-discharge polymerization is being used to form well-adhered coatings. Ion implantation is being investigated to improve certain surface properties of metals and polymers, such as hardness and wear resistance.

Active surfaces influence the biologic interaction to obtain the desired response and include enzymatic agents such as thrombolytic agents and antimicrobials that can be immobilized onto the surfaces of devices. Many methods now exist to improve biologic response by modifying surface properties, depending on what kind of substrate is modified. Structures hundreds of angstroms in dimension can be produced in block copolymers by controlling the processing conditions (i.e., annealing or slow casting the solvent solutions of the polymer). This controls phase separation within the polymer. Polyurethanes and experimental block copolymers have been shown to affect protein adsorption and cellular adhesion.[17] Utilization of the proper surfaces will allow a new control of biological interactions that will benefit the patient.

The development of biomedical materials and their incorporation in medical devices requires an interdisciplinary approach coupled with an understanding of how the device interfaces with the body.

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